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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,956	02/05/2002	Jack Barber	016556-002910US	7921

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EXAMINER	
LACOURCIERE, KAREN A	

ART UNIT	PAPER NUMBER
1635	16

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,956	BARBER ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-100* is/are pending in the application.

4a) Of the above claim(s) *1-24,51-64 and 66-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-50,65 and 71-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02-05-2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II in Paper No. 15 is acknowledged.

Claims 1-24, 51-64 and 66-70 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 15.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25-50 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25-50 of copending Application No. 09/357,741. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 25-50 are almost identical between the co-pending applications, with the difference being that the claims

of 09/351,741 are specifically limited to randomized recognition sequences, whereas the instant claims are directed to randomized binding sequences. The instant claims and the co-pending claims overlap in scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 25-33, 37-42, and 44-46, are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent No. 6,605,429 .

Claim 6 of US Patent number 6,650,429 is directed to methods of selecting a hairpin ribozyme wherein cells are transformed with a vector expressing a library of hairpin ribozymes having randomized recognition sequences and a FACS sortable reporter gene. The specification contemplates such methods wherein the vector is an AAV vector and at least 12 nucleotides are randomized and wherein the entire population of a library is used. The methods of claim 6 overlap in scope with the methods of instant claims 25-33, 37-42 and 44-46.

Claims 25-50 and 71-100 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39-68 of copending Application No. 10/613,565. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 39-68 are drawn to methods for identifying a nucleic acid molecule that modulates a process in a biological system wherein a random library of catalytic nucleic acid molecules comprising a random binding domain are introduced into a biological system and the

sequence of a nucleic acid which modulates the biological process is determined. These methods overlap in scope with the instantly claimed methods.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 86-90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 86-90 are indefinite due to the recitation "derived from". It is unclear what degree of change and type of change can occur in a vector, relative to the specific type of claimed vector recited in each of claims 86-90 such that the vector would be considered to be "derived from" the particular type of vector claimed, rather than being an entirely different type of vector. The metes and bounds of the vector used in each of the claimed methods cannot be determined and, therefore, the skilled artisan could not determine the scope of the claimed methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25-30, 33, 35, 37, 40-43, 49, 50, 65 and 71-100 are rejected under 35 U.S.C. 102(e) as being anticipated by Thompson (US Patent No. 6,183,959).

Claims 71-100 are identical to claims 1-6, 9, 10, 12-26, 30, 31, 33, 34, and 36-38 of Thompson.

Thompson discloses transforming a cell with a vector encoding a ribozyme, including hairpin ribozymes, wherein the ribozyme inhibits the expression of a target gene (see for example, columns 13 and 14), as claimed in instant claim 65.

Thompson discloses methods of identifying a nucleic acid that modulates a biological process by introducing a random library of nucleic acid catalysts into a biological system wherein the nucleic acid catalyst comprises a random substrate binding domain, wherein the binding domain comprises 9 or more random nucleotides and further wherein their random library contains all possible variants in the binding arm(s) of a particular ribozyme motif. Thompson discloses determining the sequence of at least a portion of the substrate binding domain of a nucleic acid catalyst that modulates the process. Thompson further discloses identification of the altered gene, biological systems which are bacterial, plant, mammalian, yeast or Drosophila in origin, hairpin motif ribozymes, random nucleic acid catalyst libraries encoded by expression

vectors comprising a transcription initiation and termination codon, retroviral, adenoviral, adeno-associated viral and bacterial plasmid vectors and wherein the library is a multimer random library. In column 22, lines 55-65 they further teach constitutive expression of the catalytic nucleic acid molecule, identification of specific phenotypic results and in lines 15-20 selection using a gene that confers resistance to a cytotoxic substance following transfection. The methods of Thompson include wherein the promotor is a tRNA promoter (see for example, column 8).

Therefore, Thompson anticipates claims 25-30, 33, 35, 37, 40-43, 49, 50, 65 and 71-100.

Claim 65 is rejected under 35 U.S.C. 102(b) as being anticipated by Draper et al.

Draper et al. disclose transforming cells with a vector encoding a hairpin ribozyme, wherein a cell line with altered expression of a gene is produced. The method of identifying the hairpin ribozyme does not materially change the ribozyme, therefore, transforming a cell using a vector encoding a ribozyme identified by any method is encompassed in the claims. The method steps of the method of claim 25 are not required in the method of producing a cell line of claim 65, which is only directed to a method comprising a transfection step. Therefore, Draper et al. anticipates claim 65.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-50, 65 and 71-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson (U.S. Patent 6,183,959) in view of Tuschl et al. (EMBO, Vol. 17, No. 9, pp. 2637-2650, 1998), Mirabelli et al. (U.S. Patent 5,639,595), Nigon et al. (U.S. Patent 5,252,465), Barber et al. (U.S. Patent 6,043,077).

Thompson is relied upon as set forth above. He does not specifically teach probing for the ribozymes, the claimed phenotypic differences wherein the phenotype is drug resistance and growth in soft agar or vector components including ITR's,

selectable markers including Neo^r or Hygro^r , or the promoters tRNAval, tRNAser or PGK, as instantly claimed.

Tuschl et al. is relied upon to teach use of a probing and amplification step in a method of selection of ribozymes (see page 2648, column 1).

Zambrowicz et al. is relied upon to teach the phenotypic difference, the ability to grow on soft agar (see col. 16, lines 56-66).

Mirabelli et al. is relied upon to teach the phenotypic difference, adherence (see col. 4, lines 57-65 and col. 5, lines 1-27).

Barber et al. is relied upon to teach AAV vectors with ITRs and use of tRNA promoters (see col. 17-18).

Nigon et al. is relied upon to teach selectable markers such as Neo and Hygro under expression of the SV40 promoter. (See col. 4, lines 46-68)

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to select ribozymes and the sequences they bind to taught by the methods of Thompson via (1) probing for the ribozyme as taught by Tuschl et al., (2) screening for the phenotypic differences taught by Zambrowicz et al. and Mirabelli et al., and (3) using vectors having well-known promoter components and selection systems taught by Barber et al. and Nigon et al.

One of ordinary skill in the art would have been motivated to practice the methods of Thompson broadly for any phenotypic difference as broadly claimed and disclosed by Thompson by Thompson. As such, one would have been motivated to practice the methods for the ability to grow on soft agar and loose adherence as taught

by Zambrowicz et al. and Mirabelli et al. One of ordinary skill in the art would have been further motivated to practice the methods of Thompson with viral vectors having the specific promoter, selectable marker components taught by Barber et al. and Nigon et al. since Thompson also broadly claimed and disclosed use of any such viral vector, and the claimed components, such as tRNA promoters, AAV ITRs, and selectable markers such as Neo and Hygro were well-known components of such vectors.

One of ordinary skill in the art would have had an expectation of success to practice the methods of Thompson for observation the phenotypic differences taught by Zambrowicz et al. and Mirabelli et al. since Thompson such phenotypes were known in the art as physiological differences suitable as biological readouts. Further, one of ordinary skill in the art would have had an expectation of success to substitute well-known viral vector components and vector selection systems taught by Barber et al. and Nigon et al. into any viral vector as broadly taught by Thompson since the claimed components were well-known in the art at that time.

Claim Objections

Claim 25 objected to because of the following informalities: Claim 25 is grammatically incorrect because in line 11 the recitation the article "an" does not agree with the plural noun "members". This objection would be obviated if the word "an" were amended to read "any" or the word "members" was amended to read "member". Appropriate correction is required.

Claim 55 objected to because of the following informalities: Claim 55 ends in two periods. Appropriate correction is required.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (571) 272-0759. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Lacourciere
February 19, 2004

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER